

Sub 24  
concluded

R<sub>6</sub> represents hydrogen;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

X is COOH and can originate from any C on the ring; and

n = 0-1.

✓  
Please amend claim 40 as follows:

Sub 53  
C2

40. (Amended) The method of claim 38 wherein said process is the *in vivo* modulation of lipid metabolism, *in vivo* modulation of skin-related processes, *in vivo* modulation of autoimmune diseases, *in vivo* modulation of fatty acid metabolism, *in vivo* modulation of malignant cell development, *in vivo* modulation of premalignant lesions, or *in vivo* modulation of programmed cell death.

✓  
Please cancel claims 1-3 and 10-13 without prejudice.

REMARKS

New claims 45-46 have been added with this Amendment. Support for these claims is found in numerous places in the specification, including for claim 45, for example, at pp. 9-12, and for claim 46, for example, at pp. 9-12, 68, and 97-98.

Claim 40 has been amended to specify additional processes, as described, for example, at page 83 of the specification.

In the Office Action dated May 15, 1996, claims 10-13 of this application were considered allowable. These claims have,

however, been cancelled from this application by this Amendment because these claims have now been found allowable in the parent application.

Claims 1-3 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of co-pending Serial No. 08/472,784 and Serial No. 08/485,386, as well as under § 112. Claims 1-3 have been deleted from this application and will be pursued in the first of the two above-referenced co-pending applications.

Claims 33-44 have been rejected under 35 U.S.C. § 112, second paragraph, on the premise that the term "ligand" is overly broad and indefinite and the claims should instead specifically recite the compounds intended. Applicants respectfully traverse this ground for rejection. Claims 33-44 are directed to the disclosed compositions, as well as to methods for using them, comprising the combination of two different ligands -- a first ligand which selectively activates Retinoid X Receptors (RXRs) in preference to Retinoic Acid Receptors (RARs), and a second ligand having the reverse properties of selectively activating RARs in preference to RXRs. The specification discloses such ligands and provides clear guidance on how to predictably select and assay such ligands to verify their claimed activity.

For example, at page 3, line 29 to page 4, line 1 of the specification, the compound all-trans-retinoic acid is identified as a ligand upon which the transcription-modulating activity of Retinoic Acid Receptor-alpha (RAR-alpha) depends. At page 4, lines

8-14, all-trans-retinoic acid is stated to be a natural ligand for RARs and capable of binding those receptors with high affinity, resulting in the regulation of gene expression. At page 5, lines 19-24, the compound 9-cis-retinoic acid is described as a natural endogenous ligand for Retinoid X Receptors (RXRs), able to bind and transactivate the RXRs as well as RARs, and therefore a bifunctional ligand. At pages 73-75 of the specification, compounds including 3-Methyl-TTNCB and 3-Methyl-TTNEB, among others, are disclosed which preferentially activate Retinoid X Receptors versus Retinoic Acid Receptors. Further, pp. 67-72 of the specification describes the co-transfection assay which can be used to evaluate retinoid receptor subtype selectivity of a ligand.

The specification also discloses the surprising and greater than additive effect of combining these two different types of ligands into a composition. See, for example, pp. 89-96 of the specification.

Applicants submit that the language of claims 33-44 does define the claimed invention with a reasonable degree of particularity and distinctness which reasonably apprises those of skill in the art both of the utilization and scope of what applicants regard as their invention. Accordingly, applicants request reconsideration and allowance of claims 33-34, as well as claims 45-46.

Accompanying this Response is a petition requesting a three-month extension of time to file this Response and Amendment, along with our check in the amount of \$930 for the extension fee.

The Assistant Commissioner is hereby authorized to charge any additional fees which may be required by this communication, or credit any overpayment, to Deposit Account No. 12-2475.

Respectfully submitted,

LYON & LYON

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By:

  
Hope E. Melville  
Reg. No. 34,874

LYON & LYON  
633 West Fifth Street  
47th Floor  
Los Angeles, California 90071-2066  
(213) 489-1600